Table e-1 – Characteristics of The Children and The Parents, and MR Scanner Type Across Six Genotype Groups (mean ± standard errors)

	***APOE* ε2/ε2**[§]	***APOE* ε2/ε3**	***APOE* ε3/ε3**	***APOE* ε3/ε4**	***APOE* ε4/ε4**	***APOE* ε2/ε4**	**One-way ANOVA or X^2 p-values**
Children Characteristics							
*APOE*ε genotype frequency, n (%)	2 (0.17)	141 (11.9)	733 (61.78)	259 (21.8)	21 (1.75)	31 (2.6)	0.40*
Boys /Girls	0/2	67/74	390/343	137/122	12/9	12/19	0.28
Age (years)	9.04±2.57	13.26±0.38	11.86±0.18	12.05±0.30	10.44±1.04	11.11±0.95	**0.03**
GAF_Europe**	0.60±0.40	0.60±0.35	0.65±0.01	0.59±0.02	0.35±0.07	0.71±0.07	**0.003**
GAF_Africa	0.04±0.04	0.14±0.02	0.10±0.008	0.17±0.02	0.36±0.09	0.16±0.06	**<0.0001**
GAF_American Indian	0	0.02±0.005	0.05±0.005	0.04±0.007	0.03±0.01	0.004±0.002	**0.003**
GAF_East Asia	0.29±0.29	0.22±0.03	0.15±0.01	0.16±0.02	0.24±0.08	0.12±0.05	0.16
GAF_Oceania	0.08±0.08	0.008±0.002	0.007±0.001	0.01±0.002	0.02±0.009	0.003±0.002	**0.002**
GAF_Central Asia	0	0.013±0.007	0.03±0.006	0.018±0.006	0	0.004±0.003	0.23
Parent/Guardian Characteristics							
Household Income: *1=<$5K; 6=40K-50K, 12=≥$300K*	7.00±1.00	6.74±0.22	6.90±0.09	6.52±0.16	5.48±0.46	6.84±0.41	0.07
Highest Education: *7=Professional, 4=High School Graduate, 1=<7 yrs of school*	5.5±0.50	5.77±0.10	5.86±0.04	5.61±0.08	5.19±0.26	6.07±0.20	**0.007**[‡]
Highest Occupation: *7=Higher Executives, 4=Clerical & Sales Worker, 1=Unskilled employees*	5.00±1.00	5.01±0.15	5.20±0.06	4.85±0.11	3.8±0.41	5.03±0.30	**0.001**[‡]
MR Scanners							
General Electric Medical	0	20	144	52	0	5	0.14
Philips Medical	1	25	110	46	2	2	
Siemens	1	96	479	161	19	24	

[§] Data for the ε2ε2 children were excluded from all statistical models.

* Hardy-Weinberg equilibrium was found for *APOE*ε genotype frequency (p=0.4) and for the allelic frequency at rs7412 (p=0.06). As expected, the allelic frequency at rs429358 deviates from HWE (p<0.0001).

** The number for GAF refers to the children with the particular fraction of genetic ancestry in that genotype group.

[‡] When corrected for GAF, the highest education (p=0.03) and occupation levels (p=0.04) still differ across the 5 APOE genotype groups. p-values < 0.05 were considered significant (bold font).

Table e-2. Volumes or Fractional Anisotropy in Subcortical Brain Regions That Showed Age –by-Genotype Effects

Regions Of Interest (ROI)	General Additive Models* (n=1,080)					
	Volume			Fractional Anisotropy		
	***APOEε* Effect** Estimated Mean±SD (p-value)	**Age Effect** p-value	**Age x *APOEε* Interaction** R^2 Adjusted, % Explained Deviance (p-value)	***APOEε* Effect** Estimated Mean±SD (p-value)	**Age Effect** (p-value)	**Age x *APOEε* Interaction** R^2 Adjusted, % Explained Deviance (p-value)
L_Hippocampus	0.28±0.55 (0.02)	**<0.0001**	0.418, 43.3% (0.009)	0.004±0.003 (0.12)	0.79	**0.175, 19.6% (0.01)**
R_Hippocampus	**0.50±0.55 (0.001)**	**<0.0001**	0.405, 42.1% (0.02)	0.004±0.002 (0.07)	0.55	**0.125, 15% (0.003)**
L_Thalamus	0.08±0.33 (0.27)	**<0.0001**	0.648, 65.8% (0.11)	**0.006±0.0007 (0.003)**	**<0.0001**	**0.632, 64.3% (0.01)**
R_Thalamus	0.43±0.32 (0.88)	**<0.0001**	0.670, 67.8% (0.99)	0.001±0.004 (0.60)	**<0.0001**	0.653, 66.2% (0.03)
L_Amygdala	2.57±0.25 (0.18)	**<0.0001**	0.637, 64.7% (0.99)	0.001±0.004 (0.99)	0.12	**0.209, 23.3% (0.0003)**
R_Amygdala	1.67±0.28 (0.43)	**<0.0001**	0.76, 76.6% (0.99)	0.004±0.003 (0.30)	0.28	0.177, 20.1% (0.11)

* All analyses accounted for socio-economic status, sex, genetic ancestry factor (GAF), and scanner device. All volumes were additionally adjusted for intracranial volume.

After adjustments for multiple comparisons using Holm-Bonferroni correction for the seven subcortical regions per hemisphere, p-values $\leq$ 0.0036 - 0.01 (rank ordered) were considered significant (bold font)

R^2 and% explained deviance were for the entire model

Table e-3. Age and Genotype Effects on Cortical Morphometry

Regions Of Interest (ROI)	General Additive Model* (n=1080)								
	Volume			Area			Thickness		
	***APOEε* Effect** Estimated Mean±SD (p-value)	**Age Effect** p-value	**Age x *APOEε* Interaction** R^2 Adjusted, % Explained Deviance (p-value)	***APOEε* Effect** Estimated Mean±SD (p-value)	**Age Effect** p-value	**Age x *APOEε* Interaction** R^2 Adjusted, % Explained Deviance (p-value)	***APOEε* Effect** Estimated Mean±SD (p-value)	**Age Effect** p-value	**Age x *APOEε* Interaction** R^2 Adjusted, % Explained Deviance (p-value)
R_Lateral Occipital Cortex	**532.5±342.8 (0.005)**	**<0.0001**	0.325, 34.1% (0.07)	**136±112.9 (0.005)**	**<0.0001**	0.19, 21%, (0.99)	0.02±0.02 (0.35)	**<0.0001**	0.634, 64.3% (0.99)
R_Medial Orbito Frontal Cortex	126.5±125 (0.59)	**<0.0001**	0.317, 33.3% (0.99)	**48.5±36.8 (0.004)**	**<0.0001**	0.17, 18.5% (0.99)	0.03±0.03 (0.29)	**<0.0001**	0.586, 59.6% (0.99)
R_Cuneus	118±118 (0.08)	**<0.0001**	0.258, 27.8% (0.02)	**69.2±41.3 (0.006)**	**0.0007**	0.11, 13.4% (0.99)	0.02±0.03 (0.82)	**<0.0001**	0.517, 52.9%, (0.99)
L_Inferior Parietal Cortex	345±415 (0.37)	**<0.0001**	**0.3, 31.5% (0.002)**	102.5±114.8 (0.36)	**<0.0001**	0.17,19.2% (0.02)	0.009±0.02 (0.41)	**<0.0001**	0.322,64.2% (0.05)
R_Superior Parietal Gyrus	106.2±360 (0.97)	**<0.0001**	**0.48, 49.6% (10^{-4})**	72.8±111.2 (0.88)	**<0.0001**	0.252, 27.2% (0.02)	0.008±0.02 (0.87)	**<0.0001**	0.698,7.6% (0.01)
R_Isthmus Cingulate	96.1±77.8 (0.25)	**<0.0001**	0.242, 26.1%, (0.1)	23.9±21.8 (0.25)	**0.0002**	0.135, 15.8% (0.05)	96.1±77.8 (0.59)	**<0.0001**	**0.41, 42.9% (0.0004)**
R & L_Temporal pole	55.6±47.4 (0.24)	**0.004**	0.116, 14% (0.01)	8.4±7.2 (0.17)	**<0.0001**	0.135, 15.7% (0.13)	0.01±0.04 (0.91)	**0.003**	**0.07, 8.83% (0.005)**

*All analyses accounted for socio-economic status, sex, genetic ancestry factor (GAF), and scanner device.

After adjustments for multiple comparisons using Holm-Bonferroni correction for the 20 selected ROIs per hemisphere, p-values $\leq$ 0.0013 - 0.01 (rank ordered) were considered significant (bold font)

Table e-4. Age and Genotype Effects on Cortical Morphometry only in Children with >50% European Ancestry

Regions Of Interest (ROI)	General Additive Models in European Only* (n=684)								
	Volume			**Area**			**Thickness**		
	***APOEε* Effect** Estimated Mean±SD (p-value)	**Age Effect** p-value	**Age x *APOEε* Interaction** R^2 Adjusted, % Explained Deviance (p-value)	***APOEε* Effect** Estimated Mean±SD (p-value)	**Age Effect** p-value	**Age x *APOEε* Interaction** R^2 Adjusted, % Explained Deviance (p-value)	***APOEε* Effect** Estimated Mean±SD (p-value)	**Age Effect** p-value	**Age x *APOEε* Interaction** R^2 Adjusted, % Explained Deviance (p-value)
R&L_Hippocampus	**128.7±90.2 (0.002)**	**<0.0001**	0.274 29.7% (0.02)						
R_Lateral Occipital Cortex				331.9±171.8 (0.04)	**<0.0001**	0.186 21% (0.99)			
R_Medial Orbito Frontal Cortex				**58.9±36.9 (0.0004)**	**<0.0001**	0.162 18.6% (0.99)			
R_Cuneus				55.9±62.6 (0.008)	**0.002**	0.109 13.4% (0.99)			
L_Inferior Parietal Cortex	294±390.2 (0.12)	**<0.0001**	0.34 30.7% (0.006)						
R_Superior Parietal Gyrus	403±541.8 (0.03)	**<0.0001**	**0.464** **48.1% (0.0005)**						
R_Isthmus Cingulate							0.02±0.05 (0.25)	**<0.0001**	0.408 42.5% (0.03)
R&L_Temporal pole							0.03±0.06 (0.83)	0.37	**0.0567** **8.32% (0.003)**

** Children were considered from European ancestry when GAF for European was higher than 0.5. Since no Age-by-APOE-by-European status interactions were found on all morphometric and microstructural measurements of our interest, we further analyzed the main effect of Age and APOE genotypes as well as their interactions on those measurements only in children with European ancestry. All analyses accounted for socio-economic status, sex, and scanner device.

R^2 and% explained deviance were for the entire model